IN THE EUROPEAN PATENT OFFICE

Applicant: Omeros Corporation, et al.

European Application No: 00947581.5

Int'l. Filing Date: 21 July 2000 (21.07.00)

Title: SOLUTIONS AND METHODS FOR INHIBITION OF PAIN, INFLAMMATION AND CARTILAGE DEGRADATION

Agent's File Reference No. APEP01999

DECLARATION OF STEVEN R. GOLDRING, M. D. AND MARY B. GOLDRING, Ph.D.

I DO HEREBY SOLEMNLY AND SINCERELY DECLARE AS FOLLOWS:

1. I, Steven R. Goldring, M.D., am a Professor of Medicine at Harvard Medical School, Director of Research at New England Baptist Bone and Joint Institute, and Chief of Rheumatology at New England Baptist Hospital, Beth Israel Deaconess Medical Center and New England Deaconess Hospital. I obtained my Medical Degree from the Washington University School of Medicine, completed my residency at Peter Bent Brigham Hospital, Harvard Medical School, and am certified by the American Boards of Internal Medicine and Rheumatology. I am, and for the last 29 years have been, active in research and clinical practice in specialties including osteoporosis, inflammatory arthritis and other diseases involving physiological and pathological bone remodeling. I have authored or co-authored over 108 publications and reviews in refereed journals and chapters of books in these fields, and serve on the editorial boards of *Bone* and *Journal of Bone and Mineral Research*. As part of my academic, research and hospital responsibilities, I supervise and train academicians and clinicians of less experience in my specialties. My *curriculum vitae,* including a bibliography of publications, is attached.

2. I, Mary B. Goldring, Ph.D., am an Associate Professor of Medicine (cell biology) at the Beth Israel Deaconess Medical Center and Harvard Medical School and a Senior Scientist at the New England Baptist Bone & Joint Institute. I hold a Ph.D. in Human Metabolism and Clinical Biochemistry from the University of Sheffield, England, and was a research fellow at Massachusetts General Hospital and at Harvard Medical School. I currently serve on the editorial board of *Osteoarthritis & Cartilage* and am an associate editor of the *Journal of*

Cellular Physiology. I am, and for the last 22 years have been, actively involved in research in the fields of osteoarthritis and rheumatoid arthritis, with particular research interests in the regulation of gene expression in cultured human chondrocytes, fibroblasts and osteoblasts by cytokines, growth factors and prostaglandins, and in the development of human chondrocyte culture models to study chondrogenesis, chondrocyte hypertrophy and endochondral ossification. I have authored or coauthored in excess of 160 articles and reviews in peer reviewed journals. As part of my academic and research responsibilities, I supervise and train scientists of less experience in my specialties. My *curriculum vitae,* including a bibliography of publications, is attached.

3. We have each reviewed and are familiar with the disclosure and claims contained in European Patent Application 00 947581.5 (the "Application"), corresponding to International Patent Application PCT/US00/19864. We have each been asked to express our opinions regarding certain scientific terms used in the Application. These terms include: "chondroprotective agent"; "anabolic chondroprotective agents" (also referred to in the Application as "agents that promote cartilage anabolism"); and "inhibitors of cartilage catabolism" (also referred to in the Application as "agents that inhibit unregulated or excess cartilage catabolic processes"). Specifically, we were each asked to express our opinions on whether these terms would have been readily understood and considered to be definite by one of ordinary skill, experience and expertise in the relevant scientific field, in view of the disclosure set forth in the Application, and based on public knowledge available to such individuals as of 21 July 1999. We were also asked whether such individuals would readily be able to determine whether a given therapeutic agent was an anabolic chondroprotective agent, or an inhibitor of cartilage catabolism, in view of the disclosure set forth in the Application, and using public knowledge available to such individuals as of 21 July 1999, without undue experimentation.

4. The following are our answers to the above questions, which we prepared in collaboration and which also accurately reflect our individual opinions and views, based on personal knowledge and in view of the disclosure set forth in the Application.

a. The terms "chondroprotective agent", "anabolic chondroprotective agent" and "inhibitor of cartilage catabolism" are frequently used and described in the literature, and are readily recognized by those of ordinary skill in the art. A search on PubMed (http://www.ncbi.nim.nih.gov:80/entrez) using the terms "chondroprotective OR chondroprotection" revealed 223 publications to date, including 156 publications prior to July 21, 1999. The term "chondroprotective agent" has been used to apply to catabolic enzyme inhibitors,

inhibitory cytokines, NO synthase inhibitors, cytokine receptor antagonists, and other anti-inflammatory, anti-catabolic or anabolic agents. It is generally understood that a chondroprotective agent need not necessarily target the chondrocyte.

b. The term "chondroprotective agent" is understood from the disclosure of the Application and is used therein to encompass both agents that inhibit cartilage degradation, i.e., catabolic inhibitory agents, and agents that promote cartilage synthesis, i.e., anabolic agents. The concept that agents that inhibit cartilage degradation and agents that promote cartilage synthesis may be chondroprotective was well recognized by July, 1999, as addressed in an article published in January, 1999, by M.B. Goldring (1). This article summarized the differences between catabolic factors, mainly inflammatory cytokines such as IL-1 and TNF-α, and anabolic factors, mainly growth/differentiation factors such as TGF-β, BMPs, and IGF-I, with respect to their separate effects on cartilage metabolism *in vitro* and *in vivo*. This article also suggested that catabolic factors or anabolic factors could be used as targets or agents of therapy for protecting cartilage at early stages of osteoarthritis. That catabolic and anabolic events in ostoearthritis (OA) cartilage were well recognized is also exemplified in two articles published as part of a workshop conducted in May, 1998 (2,3).

c. The term "anabolic chondroprotective agent" is used in the Application to refer to agents that promote cartilage synthetic processes. Such anabolic agents are well characterized and described in the literature. Anabolic agents have been classified as those that promote cartilage repair and/or counteract the effects of catabolic factors. Growth/differentiation factors, which participate in cartilage synthesis during skeletal development, are considered as obvious anabolic agents, since they also have direct anabolic effects on mature articular cartilage (4). The concept that an anabolic agent could be chondroprotective had been addressed prior to July, 1999 (5).

d. One of ordinary skill in the art would be able to readily determine without undue experimentation whether any given agent is an anabolic chondroprotective agent. Specific preferred methods, assays, standards and/or tests (extant as of July 21, 1999) that would be employed to determine whether a given agent is an anabolic chondroprotective agent include both *in vitro* and *in vivo* assays. The most widely used and accepted assay for determining whether an agent is anabolic for cartilage is the analysis of synthesis of cartilage-specific proteoglycans in cultures of cartilage fragments or isolated chondrocytes of bovine or human origin (4,6). Analysis of collagen types was also used widely (7). These assays involved biosynthetic labeling with [^{35}S]sulphate for proteoglycan synthesis or with [^{3}H]proline for

collagen chains, followed by precipitation of the incorporated cpm, which were measured on a scintillation counter, or separation by gel chromatography without or with Western blotting. Analysis of specific proteoglycan and collagen mRNAs had also been employed for more than a decade. Reagents had also become available for *in vivo* analysis of synthetic biomarkers in synovial fluids or sera from OA patients. These included antibodies against synthetic epitopes such as the C-propeptide of type II collagen (8) and the 846, 3B3(–), and 7D4 epitopes of aggrecan (9). These concepts have been reviewed recently (10).

e. The term "inhibitor of cartilage catabolism" is used in the Application to refer to agents that inhibit cartilage breakdown. Such catabolic inhibitory agents are well characterized and described in the literature, as reviewed (10,11). The concept that specific enzyme inhibitors could be formulated to specifically target cartilage-degrading enzymes has been around at least since the first tissue inhibitor of metalloproteinases (TIMP-1) was discovered (12). Since the MMPs (collagenase-1, MMP-1; gelatinase A, MMP-2; and stromelysin, MMP-3), which were known at that time, could degrade both collagen and proteoglycan molecules, much effort was focused on developing small molecule inhibitors that would target the functional sites of these enzymes. When additional MMPs, as well as the aggrecanases of the ADAM-TS family (13), as well as additional TIMPs, were discovered later, the task became more daunting because of structural and functional similarities among the different MMPs and toxicity at other organ sites. However, the substrate specificities, for example, of MMP-13 for type II collagen (14), have made it possible to think in terms of targeting cartilage degradation without disrupting physiological homeostasis. In addition to direct enzyme inhibitors, agents that stimulate the synthesis of enzyme inhibitors, such as TGF-β, which stimulates TIMP-1 gene expression (15), had also been considered as catabolic inhibitory agents. It is well understood by those skilled in the art that many agents such as TGF-β may have dual roles as anabolic agents and catabolic inhibitors. Inhibitors of signal transduction events controlled by p38 MAPK, JNK, and NF-κB are also considered as catabolic inhibitors since they may downregulate the expression of cartilage-degrading enzymes by chondrocytes or synovial cells (16,17).

f. One of ordinary skill in the art would be able to readily determine without undue experimentation whether any given agent is an inhibitor of cartilage catabolism. Several specific methods, assays, standards and/or tests to determine whether a given agent is an inhibitor of cartilage catabolism were available as of July 21, 1999. The most widely used by academic and pharmaceutical researchers was the assay of the release of glycosaminoglycans (GAGs), degradation products of aggrecan and other proteoglycans, from bovine cartilage fragment

cultures (18). The most common form of this assay employed 1.9-dimethylmethylene blue to spectrophotometrically determine the amount of chondroitin sulfate-containing GAGs in the culture medium (19). An agent was considered a cartilage catabolic inhibitor if it blocked the release of GAGs stimulated by IL-1 or other catabolic stimulator. More recently, antibodies that recognize specific epitopes generated by collagenase or aggrecanase-mediated breakdown of type II collagen (20) or aggrecan core protein (21) have been developed and employed for *in vitro* and *in vivo* determinations (22). The report of the Osteoarthritis Initiative Steering Group held on February 28-29, 2000 at the NIH provides a review of the literature indicating the use of such assays was well established prior to July 21, 1999 (23).

g. The patent specification accurately sets forth classes and examples of agents that are expected to be anabolic chondroprotective agents, and such classes and agents sufficiently illustrate and define this term.

h. The patent specification accurately sets forth classes and examples of agents that are expected to be chondroprotective agents that are inhibitors of cartilage catabolism, and such classes and agents sufficiently illustrate and define this term.

i. Conventional chondroprotective therapy prior to July 21, 1999 was directed to the systemic administration of chondroprotective agents that are inhibitors of cartilage catabolism, including MMP inhibitors (24) and anticytokine therapies (16). The literature also reflects research on the use of cartilage anabolic agents (25). While the literature reflects that the osteoarthritis scientific community had been well aware of the significance of both catabolic and anabolic cartilage processes (1,2,3) for some time, the therapeutic combination of a cartilage anabolic agent with an inhibitor of cartilage catabolism had not been proposed, and the local delivery of such combinations was not considered. Although it was recognized that local therapy via cell-based approaches (e.g., Carticel (26)) or *ex vivo* or *in vivo* viral delivery (e.g., IL-1ra gene therapy (27)) were potentially useful approaches, the concept that local rather than systemic delivery would be necessary for combined approaches targeting cartilage catabolism at the same time as promoting cartilage anabolism (repair) had not been proposed. The literature did not, to our knowledge, recognize that local (e.g., intra-articular) administration of an anabolic cartilage agent together with an inhibitor of cartilage catabolism would be more effective than administration of either an anabolic agent or an inhibitor of cartilage catabolism alone. Local administration of an anabolic cartilage agent together with an inhibitor of cartilage catabolism is expected, based on the disclosure of the Application and subsequent developments, to be more

effective than administration of either an anabolic agent or an inhibitor of cartilage catabolism alone.

5. Each of the undersigned makes this solemn declaration conscientiously and sincerely believing the same to be true.

6. In the event that a copy of this declaration should ever be filed in any corresponding United States Patent Application, each of the undersigned hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful, false statements and the like that are so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States code and that such willful, false statements may jeopardize the validity of the application or any patent issued thereon.

DATED this 9 day of April, 2003.

Steven R. Goldring, M.D.

DATED this 9 day of April, 2003.

Mary B. Goldring, Ph.D.

References cited in Declaration of Steven R. Goldring, M.D. and Mary B. Goldring, Ph.D.:

1. Goldring, M.B., The role of cytokines as inflammatory mediators in osteoarthritis: Lessons from animal models. *Connec. Tiss. Res.* **40:**1-11 (1999).
2. Henrotin, Y., Reginster, J.Y., Anabolic events in osteoarthritis. *Osteoarthritis Cartilage* 7(3)**:**310-2 (1999).
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5. Altman, R., Kapila, P., Dean, D., Howell, D. Future therapeutic trends in osteoarthritis, *Scand J Rheumatol* Suppl 77:37-42 (1988).
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7. Goldring, M.B., Sandell, L.J., Stephenson, M.L., Krane, S.M., Immune interferon suppresses levels of procollagen mRNA and type II collagen synthesis in cultured human articular and costal chondrocytes. *J. Biol. Chem.* **261:**9049-9056 (1986).
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9. Visco, D.M., Johnstone, B., Hill, M.A., Jolly, G.A., Caterson, B. Immunohistochemical analysis of 3-B-(-) and 7-D-4 epitope expression in canine osteoarthritis. *Arthritis & Rheumatism* **36**(12)**:**1718-25 (1993).
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12. Murphy, G., Cartwright, E.C., Sellers, A., Reynolds, J.J., The detection and characterisation of collagenase inhibitors from rabbit tissues in culture. *Biochim Biophys Acta* **483**(2):493-8 (1977).

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15. Edwards, D.R., Murphy, G., Reynolds, J.J., Whitham, S.E., Docherty, A.J., Angel, P., Heath, J.K., Transforming growth factor beta modulates the expression of collagenase and metalloproteinase inhibitor. *Embo J* **6**(7):1899-904 (1987).

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17. Goldring, M.B., Anticytokine therapy for osteoarthritis. *Expert Opin Biol Ther* **1**(5):817-29 (2001).

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Place of Birth: St. Louis, Missouri

Education:

1965	B.A., Williams College, Williamstown, Massachusetts
1969	M.D., Washington University School of Medicine, St. Louis, Missouri

Postdoctoral Training:

Internship and Residencies:

1969-1970	Straight Medical Intern, Michael Reese Hospital, Chicago, IL
1972-1973	Assistant Resident Physician, Medicine, Peter Bent Brigham Hospital, Boston, MA
1973-1974	Senior Resident Physician, Medicine, Peter Bent Brigham Hospital, Boston, MA

Clinical and Research Fellowships:

1970-1972	Public Health Service, National Institutes of Health, Bethesda, MD, Program Specialist, General Clinical Research Centers Branch
1974-1976	Clinical and Research Fellow, Arthritis Division, Massachusetts General Hospital, Boston, MA

Licensure and Certification:

1973	Massachusetts License Registration No. 35350
1974	Diplomate, American Board of Internal Medicine
1984	Diplomate, American Board of Rheumatology

Academic Appointments:

1977-1978	Instructor in Medicine, Harvard Medical School, Boston, MA
1978-1986	Assistant Professor of Medicine, Harvard Medical School, Boston, MA
1986-2000	Associate Professor of Medicine, Harvard Medical School, Boston, MA
2000-	Professor of Medicine, Harvard Medical School, Boston, MA

Hospital or Affiliated Institution Appointments:

1976-	Senior Staff Physician, Department of Medicine, New England Deaconess Hospital, Boston, MA

1976-	Visiting Senior Physician, Department of Medicine, Manchester VA Hospital
1978-	Clinical Associate, Massachusetts General Hospital, Boston, MA
1984-96	Chief of Rheumatology, New England Deaconess Hospital, Boston, MA
1995-	Chief of Rheumatology, New England Baptist Hospital, Boston, MA
1996-	Senior Staff Physician, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA
1996-	Chief of Rheumatology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1991	Visiting Professor of Orthopaedics and Rheumatology, University of Pittsburgh Medical School
1991	Visiting Professor of Orthopaedics and Rheumatology, University of Rochester Medical School
1994	Visiting Professor of Orthopaedics, University of Toronto Medical School

Hospital and Health Care Organization Service Responsibilities:

1984-88	Vice Chairman, General Medical Staff, New England Deaconess Hospital
1986-89	Medical Executive Board, New England Deaconess Hospital
1986-89	Chairman, Credentials Committee, New England Deaconess Hospital
1998-	Member, Musculoskeletal Service Line Planning Work group, CareGroup

Major Administrative Responsibilities:

Local:

1976-97	Supervisor Medical Residents Affiliated Hospital Rotations, New England Deaconess Hospital, Boston, MA
1976-97	Co-Chairman, American Board of Internal Medicine Clinical Evaluation Committee for Medical Residents, New England Deaconess Hospital, Boston, MA
1984	Chief of Rheumatology, New England Deaconess Hospital
1984-88	Vice Chairman, General Medical Staff, New England Deaconess Hospital
1986-89	Medical Executive Board, New England Deaconess Hospital
1989-93	Chairman, Credentials Committee, New England Deaconess Hospital
1993	Co-director, Musculoskeletal Block, Pathophysiology, HMS II
1995-	Chief of Rheumatology, New England Baptist Hospital
1995-	Vice Chairman, New England Baptist Bone and Joint Institute, New England Baptist Hospital
1996-	Chief of Rheumatology, Beth Israel Deaconess Medical Center
1997-	Director of Research, New England Baptist Bone and Joint Institute, Harvard Institutes of Medicine, Harvard Medical School
1997, 98	Co-Director, Harvard Medical School, Advances in Rheumatology Course
1998	Co-Chairman, Translational Research Committee, Beth Israel Deaconess Medical Center
1999-	Co-director, Musculoskeletal Block, Pathophysiology, HMS II
2000-	Senior Fellow for the Executive Committee and Rheumatology/Medicine, Cannon Society, Harvard Medical School
2001	Subcommittee of Professors, Harvard Medical School

National:

1991-93	National Research Grants Subcommittee (Cell Biology), Arthritis Foundation
1993	Vice Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth
1995	Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth
1996	Program Chairman, Annual Meeting of the American Society of Bone and Mineral Research
1997-	Secretary Treasurer, American Society of Bone and Mineral Research
1998	Co-Chairman, Keystone Conference, Pathogenesis of Rheumatoid Arthritis
2000	Member, Finance Committee, FASEB
2001	Co-Chairman, American College of Rheumatology, Annual Basic Research Conference

Government:

1990-93	Materials Science Study Section, National Institutes of Health, Bethesda, MD
1995-99	Orthopaedics and Musculoskeletal Study Section, National Institutes of Health
1997-99	Chairman, Orthopaedics and Musculoskeletal Study Section, National Institutes of Health
1999	National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health Long-Range Planning Panel on Orthopaedics
2000	Vice-Chairman, National Institutes of Health, Consensus Development Panel on Osteoporosis

Foundation:

1991-94	Chairman, Medical and Scientific Advisory Committee, Arthritis Foundation, Massachusetts Chapter
1991-	Trustee, Arthritis Foundation, Massachusetts Chapter
2000-	Chairman, Massachusetts Chapter of the Arthritis Foundation

Major Committee Assignments:

Medical School:

1987-98	Member, Dean's Committee, Harvard Medical School, Veterans Administration Affiliated Hospitals Program, New England Deaconess Hospital
1999-	Module II, Curriculum Design Group, Harvard Medical School

Hospital:

1976-98	Medical Advisory Committee, Department of Medicine, New England Deaconess Hospital, Boston, MA
1976-98	Intern Selection Committee, Department of Medicine, New England Deaconess Hospital, Boston, MA
1993-97	Member, Credentials Committee, New England Deaconess Hospital
1994-97	Member, Committee on Research, Massachusetts General Hospital
1997-	Member, Research Council, Beth Israel Deaconess Medical Center

Affiliated Institution:

1990-97	Member, Research and Development Committee, Manchester Veterans Administration Hospital
1993-	Scientific Advisory Committee, University of Connecticut, Osteoporosis Center Grant
1995	Scientific Advisory Committee, Cornell Medical College, Multipurpose Arthritis Center

National and Regional:

1989-91	Education Committee, American Society of Bone and Mineral Research
1983,85,87, 92	Program Committee, American Society of Bone and Mineral Research
1993, 97, 99	Abstract Selection Committee, American College of Rheumatology Annual Meeting
1993, 95	Abstract Selection Committee, Orthopaedic Research Society Annual Meeting
1995	Primer Three Task Force, Education Committee, American Society of Bone and Mineral Research
2000	Massachusetts Arthritis Planning Project Committee
2000	Member, Scientific and Clinical Review Board of the Canadian Arthritis Network

Professional Societies:

1976-	Member, American College of Rheumatology
1976-	Member, American Federation of Clinical Research
1978-	Member, American Society of Bone and Mineral Research
1989-	Member, Orthopaedic Research Society
1989-	Member, American Society for Cell Biology
1996	International Society of Bone and Mineral Research

Editorial Boards

1991-	Editorial Board: Bone
1991-93	Associate Editor: Bone
1991-	Editorial Board: Journal of Bone and Mineral Research
1995	Section Editor: Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism (3rd ed)
1996	Editorial Board: Journal of Biomedical Materials Research
1998	Section Editor: Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism (4th ed)
1999-	Associate Editor, Arthritis Research

Awards and Honors:

1969	Upjohn Award for Research in the Field of Metabolism
1985	Carol Nachman Prize in Rheumatology, West Germany (shared with S.M. Krane, E.P. Amento, and J-M Dayer)
1989	Tullis Research Award: New England Deaconess Hospital
1992	Paget's Disease Foundation Research Award
1993	James H. Fairclough, Jr. Award, Massachusetts Chapter, Arthritis Foundation

1993	Vice Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth
1994	Paget's Disease Foundation Research Award
1995	Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth
1996	Program Chairman, Annual Meeting of the American Society of Bone and Mineral Research
1997-	Secretary Treasurer, American Society of Bone and Mineral Research
1997-	Chairman, Orthopaedics and Musculoskeletal Study Section, National Institutes of Health
1998	Co-Chairman, Keystone Conference, Pathogenesis of Rheumatoid Arthritis
1999	Marian Ropes Award, Arthritis Foundation, Massachusetts Chapter

Part II: Research, Teaching, and Clinical Contributions

A. Narrative report of Research

The research efforts in the laboratory have focused on dissecting the cellular and molecular mechanisms involved in the regulation of physiological and pathological bone remodeling. The ultimate goal of these studies has been to develop more effective and direct therapeutic strategies for blocking bone loss in disorders such as osteoporosis, inflammatory arthritis and malignancies. In the early 1990s, the laboratory successfully cloned the human calcitonin receptor. Expression of this receptor definitively identifies the osteoclast which is the principal cell type responsible for bone resorption. More recently, the osteoclast-specific promoter of the calcitonin receptor has been cloned and this has permitted direct examination of the mechanisms regulating osteoclast differentiation and activation at a molecular level. Reagents and molecular approaches derived from these studies have been used to study several human models of pathological bone loss, including rheumatoid arthritis and malignancies that affect the skeleton. These studies have been extended to include the investigation of the role of cytokines and related soluble mediators of inflammation on osteoclast-mediated bone loss in inflammatory arthritis and malignancies. In addition, investigations have included the evaluation of the effects of orthopaedic implant biomaterials used for total joint replacement and/or bone augmentation or substitution. Research has been directed at characterization of the molecular mechanisms and cell-associated signaling pathways by which foreign implant biomaterials modulate cell and tissue responses. This information is of critical importance for the development of more effective strategies for treating end-stage destructive arthritis and for creating improved approaches for bone allografting and augmentation in conditions of skeletal insufficiency.

B. Funding Information

Research Funding Information:

Past:

1984-89	NIH PO1 AR0364-27 Project #7: Investigator Study of Mesenchymal Tissues & Their Diseases; Project # 7: Skeletal Cell Differentiation and Responses	
1988-93	NIH RO1 AR39515 Biochemical and Cellular Responses to Biomaterials	P.I.
1989-92	Zimmer Inc. Cell Culture Study of Orthopaedic Implants	P.I.

1989-94	NIH PO1 AR0364-31 Project #7: P.I. Study of Mesenchymal Tissues & Their Diseases; Project # 7: Skeletal Cell Differentiation and Responses	
1992-93	NIH DK43351-02 P.I. Pilot Feasibility Study: Calcitonin and Related Receptors in the GI Tract; Center for the Study of Inflammatory Bowel Disease	
1994-98	NIH RO1 DK46773 P.I. Calcitonin Receptor Gene Expression	
1994-98	NIH P01 AR03564-35 Project #4: P.I. Study of Mesenchymal Tissues & Their Diseases; Project #4: Function of Calcitonin Receptors	
1994-98	NIH P01 AR03564-35 Project #5: P.I. Study of Mesenchymal Tissues & Their Diseases; Project #5: Calcitonin Receptors in Development	
1995	NIH 1R13 AR43569-01 P.I. Conference on the Cell and Molecular Biology of Bones and Teeth	
1995-96	Pfizer Central Research Division P.I. Mechanism of Action of Calcitonin and the Development of Models for Defining the Mechanism of Refractoriness	
1995-96	NIH SBIR 94-3 Consultant Surface Modification to Improve Osseous Integration	
1997-98	Advanced Bio-Surfaces, Inc. Polymeric Wear Debris	
1998-02	NIH RO1-AR45421-01 Co-Investigator Regulation of the Murine Calcitonin Receptor Gene	
1999-02	Millennium Pharmaceuticals P.I. Molecular Regulation in Rheumatoid and Osteoarthritis	

Active:

1999-04	NIH RO1-AR45472-01 P.I. Cellular Responses to Inorganic Particulates	
1998-03	NIH R01-DK46773-05 P.I. Calcitonin Receptor Gene Expression	

C. Report of Current Research Activities

Bench Research:

Cellular Responses to Inorganic Particulates P.I.
Regulation of the Murine Calcitonin Receptor Gene Co-P.I.
Calcitonin Receptor Gene Expression in Human Disorders P.I.
Characterization of Factors Regulating Osteoclast Differentiation P.I.
Mechanisms of Bone Loss in Inflammatory Diseases P.I.
Development of Strategies for Preventing Orthopaedic Implant Failure P.I.

D. Report of Teaching

1. Local Contributions

a. Harvard Medical and Dental School Courses:

1976-	Musculoskeletal Block, Pathophysiology, HMS II tutor (23 years); 6-15 students 12-15 hours/year
1976-95	Introduction to Clinical Medicine, Musculoskeletal Exam Instructor (19 years); 6-10 students 3 hours/year
1976-90	Introduction to Clinical Medicine, HMS II Preceptor (14 years); 2 students/year 12-15 hours/year
1976-	Attending Physician, Medical Service, New England Deaconess Hospital (Beth Israel Deaconess Medical Center) 3-4 medical residents, 1 month/year
1976-	Rheumatology Division Lectures, New England Deaconess Hospital (Beth Israel Deaconess Medical Center) Organizer and Presenter; 20-25 residents; 4 hours/year
1976-	Medical Residency Elective in Rheumatology, New England Deaconess Hospital (Beth Israel Deaconess Medical Center) Attending Physician; 6-10 residents/year 15-20 hours/year
1976-90	Medical Interns or Residents Report, New England Deaconess Hospital (14 years) Discussion Leader; 10-15 residents or interns 5-15 hours/year
1990-	Musculoskeletal Block, Pathophysiology, HMS II Lecturer (9 years); 160 students 1-2 hours/year
1993	Endocrinology Block, Pathophysiology, HMS II Lecturer (1 year); 160 students 1 hour/year
1990-	Ward Medicine Clerkship, HMS III or IV Attending Physician (9 years); 1-2 students/year 50 hours/year
1990-	Oral Biology Course, Harvard Dental School, Graduate School Program Lecturer (9 years); 40-50 students 2 hours/year
1995-	Ambulatory Primary Care Elective, HMS II (4 years) Tutor; 2 students/yr 10 hours/yr

1995-	Rheumatology Division In-patient Consult Service, Beth Israel Deaconess Medical Center (3 years) Attending Physician; 3-4 medical residents, rheumatology fellow 40 hours/year
1996-	Rheumatology Division, Fellow Supervision, Out-patient practice, Beth Israel Deaconess Medical Center (3 years) Attending Physician; 1 rheumatology fellow 25 hours/year

b. Graduate Medical Courses

1986, 90, 91	Lecturer, Advances Total Hip Replacement, Harvard Medical School
1996, 1999	Lecturer, Total Knee Replacement, Harvard Medical School
1997, 98	Co-Director, Lecturer, Harvard Medical School, Advances in Rheumatology Course
1997-	Lecturer, Update and Review of internal Medicine, University of New Mexico Health Science Center, Beth Israel Deaconess Medical Center

e. Advisory and Supervisory Responsibilities:

1988-	Harvard Dental School, Doctor of Medical Science Program Supervisor; total of 6 students have completed doctoral program
1994-	Harvard Medical School; Student Research Fellowship Supervisor; 1 student
1989-	Massachusetts Arthritis Foundation Summer Student Research Fellowship Program Supervisor; 7 students; 1/year
1995	Senior Fellowship; NIH-Individual Research Service Award Supervisor for Professor George Baran for sabbatical training in biomaterials/cell research

f. Leadership roles:

1993	Musculoskeletal Block, Pathophysiology, HMS II Co-director; 160 students 20 hours/year
1997, 98	Co-Director, Harvard Medical School, Advances in Rheumatology Course
1999-	Co-Director, Musculoskeletal Block, Pathophysiology, HMS II; 160 students; 40 hours/year

2. Regional, National or International Contributions

a. Invited Presentations

1976-	**Arthritis Grand Rounds:** Brigham and Women's Hospital, Massachusetts General Hospital, University of Massachusetts Medical Center, Boston University Medical Center, New England Medical Center. Presentations given multiple different years
1976-	**Medical Grand Rounds:** New England Deaconess Hospital, Faulkner Hospital, Spaulding Rehabilitation Hospital, St. Elizabeth's Hospital, Massachusetts General Hospital, University of Connecticutt Medical Center. Georgetown Medical Center, George Washington University Medical Center. Presentations given multiple different years

1976-	**Endocrine Grand Rounds:** Beth Israel Hospital, New England Deaconess Hospital, Brigham and Women's Hospital, University of Connecticutt Medical Center, Washington University Medical School. Presentations given multiple different years
1976-	**Orthopaedic Grand Rounds:** New England Baptist Hospital, Brigham and Women's Hospital, Massachusetts General Hospital, New England Medical Center. Presentations given multiple different years
1985,86	Speaker, Annual Course, Total Hip Replacement, Harvard Medical School, Boston, MA
1988, 89	Speaker, Current Concepts in Rheumatoid Arthritis, Allegheny General Hospital, Pittsburgh, PA
1989	Speaker, Gordon Research Conference, Molecular Biology of Bones and Teeth
1990	Speaker, Bone/Implant Interface Session, Gordon Research Conference on Bioengineering and Orthopaedic Sciences
1990,92	Speaker, Advances in Mineral Metabolism Conference, Aspen CO
1990,92	Lecturer Harvard Medical School, Advances in Rheumatology Course
1991	Speaker, Gordon Conference on Calcium-Phosphates
1991	Lecturer, Harvard Medical School, Orthopaedic Knee Course
1991	Lecturer, Contemporary Issues in Osteoarthritis, Boston, MA, Sponsored by the Arthritis Foundation
1991	Speaker, Workshop on Cloning and Structure of Calciotropic Hormone Receptors, American Society of Bone and Mineral Research Annual Meeting, San Diego, CA
1991	Speaker, Rhone-Poulenc Symposium. "Calcitonin: 30th Anniversary, Present Applications and Future Uses", San Diego, CA
1991	Speaker, 8th Annual State-of-the-Art in Total Joint Replacement Symposium, Scottsdale, AZ
1991	Speaker, Skeletal Tissue Workshop, Annual Meeting of the American Society of Cell Biology, Boston, MA
1992	Speaker, 3rd Asian Symposium on Osteoporosis, Singapore and Taipei
1992	Speaker, Bristol-Myers Squibb/Zimmer Orthopaedic Research Symposium on Biological, Material and Mechanical Considerations of Joint Replacement, San Antonio, TX
1992	Speaker, XIth International Conference on Calcium Regulating Hormones, Florence, Italy
1992	Speaker, Winter Rheumatology Symposium, American College of Rheumatology, Snowmass, CA
1992	Speaker, Annual Endocrine Society Meeting, Workshop on Peptide Hormone Receptors
1992	Speaker, Ninth International Congress of Endocrinology, Nice, France
1993	Speaker, XXIIIrd European Symposium on Calcified Tissues, Heidelberg, Germany
1993	Speaker IInd Workshop on Osteobiology; Parma, Italy
1993	Speaker, Sandoz Workshop on Cytokines and Bone Metabolism, American Society of Bone and Mineral Research, Minneapolis, MN
1993	Speaker, XIIth International Congress of Nephrology, Jerusalem, Israel
1993	Speaker, Portland Bone Symposium, Oregon Health Sciences University, Portland OR
1993	Speaker, Bristol-Myers Squibb/Zimmer Orthopaedic Research Symposium, Current Concepts in Total Hip Revision Surgery, Chicago, IL
1993	Speaker, International Conference on Rheumatoid Arthritis: Susceptibility, Causation, Pathobiology, and Treatment, Stanford University Medical Center, Palo Alto, CA

1994	Speaker, Plastic and Reconstructive Surgery Grand Rounds, Massachusetts General Hospital
1994	Speaker, 1994 Hard Tissue Workshop, Sun Valley ID
1994,95	Speaker, Plastic and Reconstructive Surgery Grand Rounds New England Deaconess Hospital
1995	Speaker, American College of Rheumatology Conference on Diagnosis and Treatment of Osteoporosis, Los Angeles, CA
1995	Speaker, National Biomedical Engineering Society Meeting, Boston, MA
1995	Speaker, Advances in Musculoskeletal Disorders, Otto E. Aufranc Orthopedic Alumni Meeting, Boston, MA
1995	Speaker, Lower Extremities Lecture Series, New England Deaconess Hospital
1995	Speaker, International Symposium on Bone and Soft Tissue Allografts, Washinton, D.C.
1995	Speaker, Working Group on Aging and the Human Skeleton, Annual Meeting of the American Society of Bone and Mineral Research, Baltimore, MD
1995	Speaker Biologic Agents in Autoimmune Disease IV, Arthritis Foundation, San Francisco, CA
1995	Speaker, Gordon Conference on Biocompatibility and Biomaterials
1996	Speaker, Japanese Bone and Mineral Research Society, Osaka, Japan
1996	Speaker, American College of Rheumatology, Board Review Course, Orlando, FL
1997	Speaker, Gordon Research Conference on Periodontal Diseases
1996, 97	Lecturer, Boston Bone Pathology Course, Harvard Medical School, Boston, MA
1997-00	Lecturer, Update and Review of Internal Medicine, University of New Mexico/BIDMC
1997	Speaker, Second International Conference on Osteoporosis, Osaka, Japan
1997	Keynote Lecturer, Ninth Annual Conference and Workshop, Texas Mineralized Tissues Society
1998	Speaker, Annual American Gastroenterological Association, Symposium on Steroid Induced Bone Loss, New Orleans, LA
1998	Speaker, Advances in Rheumatology Course, Harvard Medical School
1998	Speaker, Sixth Annual Meeting Chronic Inflammation, London, England
1999	Speaker, Fifth International Symposium on the Immunotherapy of the Rheumatic Diseases, Cyprus
2000	Speaker, Advances in Targeted Therapies, Miami, Fl
2000	Speaker, Biologic Therapeutics Study Group, American College of Rheumatology, Philadelphia, PA
2000	Speaker, Cell Contact Interactions in Rheumatology, London, England
2001	Speaker, American College of Rheumatology Clinical Symposium: Joint Damage in rheumatoid Arthritis, San Francisco, CA
2001	Speaker, 3rd Joint Course in Advanced Immunology and Rheumatology, Nottwil, Switzerland
2001	Speaker, American Academy of Orthopaedic Surgeons/National Institute of Health, 2001 Molecular Biology Workshop. Scottsdale, AZ
2001	Speaker, American Academy of Allergy, Asthma and Immunology. Biologic Response Modifiers in Autoimmune Diseases, New York, NY
2002	Keynote Speaker, Canadian Arthritis Network Annual Conference, Calgary, AB, Canada
2002	Speaker, Annual European Congress of Rheumatology, Stockholm, Sweden
2002	Speaker, Annual Australian & New Zealand Bone and Mineral Society, Adelaide, Australia

2002 Speaker, 2002 World Congress on Osteoarthritis, Sydney, Australia

b. Professional Leadership Roles:

1991,92, 99 Session Chairman, Advances in Mineral Metabolism, Aspen, CO

1991 Workshop Organizer, Mechanical and Cellular Factors Mediating Bone Repair and Remodeling in Arthroplasty and Fracture Repair, Combined Meeting of the Orthopaedic Research Societies of USA, Japan and Canada, Banff, Canada

1991 Co-Chairman, Working Group on Particulate Biomaterials, Orthopaedic Research Society, Anaheim, CA

1991 TGF-β and Bone Advisory Panel, Genetech, San Francisco, CA

1991 Session Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth

1992 Session Chairman, Bone/Implant Interface, Gordon Research Conference on Bioengineering and Orthopaedic Sciences

1992 Organizer, Clinical Symposium on Total Joint Replacements, 56th Annual Scientific Meeting American College of Rheumatology, Atlanta, GA

1993 Vice Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth

1994 Panel Member, NIH Consensus Development Conference on Optimal Calcium Intake, Bethesda, MD

1994 Speaker, NIH Consensus Conference on Total Hip Replacement, Bethesda, MD

1994 Speaker, NIH Workshop on TMJ Alloplastic Implants and Local/Systemic Responses: Observations and Needs

1995 Session Chairman, AAOS & NIH Workshop on Considerations of Implant Wear for the Future of Total Joint Replacement, Oak Brook, IL

1995 Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth

1996 Program Chairman, American Society of Bone and Mineral Research Annual Meeting

1997, 98 Co-Director, Harvard Medical School, Advances in Rheumatology Course

1997 Co-Chairman Keystone Conference: Pathogenesis of Rheumatoid Arthritis

1997-99 Chairman, Orthopaedics and Musculoskeletal Study Section, National Institutes of Health

1998 Organizer, Workshop: Implant Loosening. Orthopaedic Research Society Meeting

1998- Co-Director, Musculoskeletal Block, Pathophysiology, Harvard Medical School

1999 Session Chairman, Gordon Research Conference, Molecular Biology of Bones and Teeth

1999 Scientific & Medical Advisory Board of the Canadian Arthritis Network

1999 National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health Long-Range Planning Panel on Orthopaedics

2000 Vice-Chairman, National Institutes of Health, Osteoporosis Consensus Development Panel

2000 Session Chairman and Speaker, AAOS/NIH Orthopaedic Implant Wear 2000 Workshop, Chicago, IL

2000	Session Chairman, Interpretations of the Impact of Anti-Rheumatic Therapies on Radiographic Progression of Rheumatoid Arthritis, National Institutes of Health, Bethesda, MD
2001	Co-Chairman and Speaker, American College of Rheumatology, Annual Basic Science Research Symposium, San Francisco, CA.
2002	Chairman, ASBMR/ACR Joint Symposium on Bone Loss Associated with Inflammatory Conditions, Annual ASBMR Meeting, San Antonio, TX.

Name: Mary Brennan Goldring (previously McGuire) January 27, 2003

Address: 30 Vista Avenue, Auburndale, MA 02166

Date of Birth: April 18, 1947

Place of Birth: Reno, Nevada

Education:

1968 B.A. University of Oregon, Eugene (Biology, Honors College)
1981 Ph.D. University of Sheffield, England (Human Metabolism and Clinical Biochemistry)

Postdoctoral Training:

Research Fellowship:

1982-1984 Research Fellow in Medicine (Connective Tissue Structure, Function and Diseases-USPHS Training Grant), Massachusetts General Hospital; Research Fellow in Medicine, Harvard Medical School

Academic Appointments:

1984-1985 Instructor in Medicine, Harvard Medical School, Boston, MA
1985-1989 Assistant Professor of Medicine (Cell Biology), Harvard Medical School.
1985-1993 Faculty Member, Program in Cell & Developmental Biology, Harvard Medical School.
1989- Associate Professor of Medicine (Cell Biology), Harvard Medical School

Hospital Appointments:

1982-1984 Research Fellow in Medicine, Massachusetts General Hospital
1984-1991 Assistant in Biology, Massachusetts General Hospital
1991- Associate Biologist, Massachusetts General Hospital
1997- Senior Scientist, New England Baptist Bone & Joint Institute, Beth Israel Deaconess Medical Center

Other Professional Positions:

1969-1971 Peace Corps Volunteer, Math and Science Teacher Training Program, Peru

1972	Research Technician to Dr. E.C. LeRoy, Arthritis Research, Columbia University College of Physicians and Surgeons, New York City
1972-1976	Research Assistant to Dr. D.R. Robinson, Arthritis Research Unit, Massachusetts General Hospital, Boston, MA
1978-1982	Research Assistant, Department of Human Metabolism & Clinical Biochemistry, University of Sheffield Medical School, Sheffield, UK (Dr. R. Graham G. Russell, Supervisor)

Awards and Honors:

1965-1969	Max C. Fleischmann Foundation Scholarship (State of Nevada)
1968	National Science Foundation Undergraduate Research Participant
1967-1968	Phi Delta Upsilon
1968-1969	Mortar Board
1984-1987	New Investigator Award (NIADDK-AM-34390)
1989	Young Investigator Award, Conference on Advances in Mineral Metabolism
1990	Arthritis Foundation Massachusetts Chapter 3-month Student Fellowship for Marc Paradis
1992	Ann Doner Vaughan Kappa Delta Award, Orthopaedic Research Society for paper entitled "Expression of Collagen and Aggrecan Genes During Skeletal Development and Growth: Control at Transcription and Post-transcription" by Linda J. Sandell, Maureen Ryan, James R. Robbins, James Sugai, Steve Trippel and Mary B. Goldring.
1994	Arthritis Foundation Massachusetts Chapter 3-month Student Fellowship for Ajay Mathur
2001	Arthritis Foundation Massachusetts Chapter 3-month Student Fellowship for Alexa Simon

Major Committee Assignments:

National and Regional:

1990-1994	NIH Oral Biology and Medicine-2 (OBM-2) Study Section
1991-1995	Editorial Board, Arthritis & Rheumatism
1992-1993	Coordinator, Cartilage Study Group, Annual Meeting of the American College of Rheumatology
1992-	Editorial Board, Osteoarthritis & Cartilage
1992-1996	Editorial Board, Agents & Actions
1994-	NIH Reviewers Reserve
1994-1997	Arthritis Foundation Molecular Biology/Genetics Study Section (Chair, 1996-97
1998-2001	Education Committee, American Society for Bone & Mineral Research
2000-2003	Annual Meeting Planning Committee, American College of Rheumatology

2000-2002 Abstract Selection Committee, American College of Rheumatology: (Category Chair: Cartilage Biology & Pathogenesis of Osteoarthritis)
2002- Associate Editor, Journal of Cellular Physiology

Harvard Medical School:

1984-1987 Faculty Member, Fuller Albright Society, Harvard Medical School
1991-1993 Admissions Committee, Division of Cell and Developmental Biology.
1991 Conference leader, Molecular Biology of the Cell, 200 B, Division of Cell and Developmental Biology.
1991-1992 Clinical or hospital faculty delegate (second alternate), for the Division of Medical Sciences at meetings of the Faculty of Arts and Sciences.
1992-1996 Clinical or hospital faculty delegate (first alternate), for the Division of Medical Sciences at meetings of the Faculty of Arts and Sciences.
1994-1995 Faculty Member, Graduate Program in Biological and Biomedical Sciences (Pathology), Harvard Medical School.
1994-1997 Mentor, HST160 Medical Genetics course
1994-1999 Thesis Advisory Committee of Paul J Fanning, BBS Program
1994-1996 Thesis Advisor, Harvard University Biology Undergraduate Program, Biology 90r (Supervised Research)
2001- Masters Thesis Advisor, Alexander B. Waldman, D.M.D., Harvard University School of Dental Medicine

Hospital:

1985-1997 Member, Subcommittee on Review of Research Proposals, Massachusetts General Hospital
1986-1987 Member, MGH Committee on Research
1987 Organizer, MGH Research Lecture Series (Spring), "Biochemistry and Molecular Biology of Extracellular Matrix Proteins"
1991-1997 Affiliated Investigator, Center for the Study of Inflammatory Bowel Disease, Daniel K. Podolsky, M.D., Program Director, MGH
1992-1996 Member, MGH Committee on Research (COR)
1996- Faculty Sponsor, NIH Training Grant in Rheumatology, Allen C. Steere, MD, Director, New England Medical Center
1997-2000 Affiliated Investigator, Center for Engineering in Medicine, Martin L. Yarmush, MD, PhD, Director, MGH
1998 Member, BIDMC Junior Investigator Award Review Committee
1998-1999 Member, BIDMC Infrastructure Committee

Memberships in Professional Societies:

American Association for the Advancement of Science
The British Society for Rheumatology
American Society for Bone and Mineral Research
American College of Rheumatology

American Society for Cell Biology
Orthopaedic Research Society
New York Academy of Sciences
Osteoarthritis Research Society International
Society for In Vitro Biology
International Society for Matrix Biology
American Society for Matrix Biology
International Bone & Mineral Society
International Cartilage Repair Society

Peer Review:

Grants (External Consultant or Ad Hoc Reviewer):

1989	NHBLI: RFA on "Molecular and Cellular Biology of Cardiac Interstitium"
1989	NIDR: Craniofacial Anomalies Research Center
1989-	The Arthritis Society (Canadian)
1990- 1991	Scleroderma National Grants Review
1991-	Veteran's Health Services and Research Administration Grants Review
1991-1992, 1998:	DEA/NIDDK: Site visit teams for Program Project "Model Systems Toward Development of Human Gene Therapy", Joseph C. Glorioso, P.I., University of Pittsburgh
1992-1993	NIAMSD: Site visit teams for Multipurpose Arthritis Centers, Duke University and University of Pittsburgh
1993-	Ad Hoc Review Committees for NIAMS and NIDDK
1993-1994	The Israel Science Foundation
1994-	The Wellcome Trust
1994	Swiss National Science Foundation
1994, 1997	Biological & Physiological Sciences Special Emphasis Panel for SBIR/STTR Grant Applications
1994-1997	Arthritis Foundation Molecular Biology /Genetics Study Section (Chair, 1996-97)
1997	Texas Higher Education Coordinating Board
1998	NASA Biotechnology Cell Science Panel
2001	NASA Cellular Biotechnology & Tissue Engineering Panel
2002-	Orthopaedic Research and Education Foundation

Journals:
Biochimica Biophysica Acta
Journal of Cell Biology
Endocrinology
Journal Biological Chemistry
Matrix Biology
Journal of Clinical Investigation
Arthritis and Rheumatism (Member, Editorial Board, 1991-1995)
FASEB Journal
Molecular Neurosciences

Osteoarthritis & Cartilage (Member, Editorial Board, 1992-present)
Agents and Actions (Member, Editorial Board, 1992-1996)
Endocrinology Journal
American Journal of Physiology
Journal of Orthopaedic Research
Clinical Orthopaedics
Experimental Cell Research
Journal of Cellular Physiology (Associate Editor, 2002 – present
FEBS Letters
Nucleic Acids Research
Journal of Biological Chemistry
Molecular Cell Biology

Abstract selection committees:

1993-	Orthopaedic Research Society, Program Committee, Adjunct Member
1994-97	American Society for Bone and Mineral Research, Scientific Program Committee
1994-	American College of Rheumatology, Abstract Selection Committee
2002	Osteoarthritis Research Society International

Major Research Interests:

1. Regulation of gene expression in cultured human chondrocytes, fibroblasts, and osteoblasts by cytokines, growth factors and prostaglandins with focus on signaling pathways and transcription factors that target collagen and other cell-specific genes.
2. Development of human chondrocyte culture models to study chondrogenesis, chondrocyte hypertrophy, and endochondral ossification with potential application to cartilage repair mechanisms in osteoarthritis.

Research Funding Information:

Past:

1984-1987	New Investigator Research Award, USPHS Grant Award AM-34390-01-03. National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases: "Activation of Human Chondrocytes"
1988-1991	NIH Research Grant: "Collagen Gene Expression in Chondrocytes in Inflammation" (R01-AR34390-04-06)
1988-1989	Wyeth Ayerst Laboratories: "The Effects of Etodolac on Connective Tissue Inflammation"
1989-1993	NIH Program Project (AR-03564-30-34) "Studies of Mesenchymal Tissues and Their Diseases." Program Director: Stephen M. Krane. Principal Investigator of Project 2. "Collagen Synthesis in Inflammation"
1991-1993	G.D. Searle & Co. - Arthritis and Prostaglandins Research Challenge: "Regulation of Cartilage Collagen Gene Expression by Cytokines and Prostaglandins"

1991-1992 Biomedical Research Support Grant (2 S07 RR05486-29) from Massachusetts General Hospital: "Collagen Gene Expression in Chondrocytes in Inflammation"

1991-1992 The Upjohn Company: "Regulation by IL-1 of Cartilage-Specific Collagen Gene Expression in Human Chondrocytes: Use of Flurbiprofen to Study Modulation by Prostaglandins"

1992-1994 Osteoarthritis Sciences, Inc.: "Development of Immortalized Human Chondrocytes as Target Cells for Cytokines"

1993-1996 Arthritis Foundation Biomedical Science Grant" "Cytokine Regulation of Type II Collagen Gene Expression in Human Chondrocytes"

1993-1997 NIH Program Project (AR-03564-35-38) "Studies of Mesenchymal Tissues and Their Diseases." Program Director: Stephen M. Krane. Principal Investigator of Project 3. "Collagen Synthesis in Inflammation"

1997-1998 SmithKline Beecham "Development of a Human Chondrocyte Culture Model for Study of Collagen Degradation"

1997-2000 Arthritis Foundation Biomedical Science Grant: "Signaling Pathways in Chondrocyte-Specific Gene Expression"

1998-2002 NIH Research Grant (R01 AR 45378): "Regulation of Matrix Gene Expression in Human Chondrocytes".

Current:

2000-2003 Arthritis Foundation Biomedical Science Grant
National and Massachusetts Chapter (Eleanor Farrington Trust)
"Signaling Pathways in Chondrocyte-Specific Gene Expression

2002-2007 NIH Research Grant (R01 AG22021): "Role of ESE1 Regulation of Type II Collagen in Cartilage"

Teaching Experience:

1969 Intern Teacher in Biology, The Lawrenceville School Summer Session, Lawrenceville, New Jersey

1969-1971 Peace Corps Volunteer, Math and Science Teacher Training Program Peru

1978-1982 Supervision of the research programs of postgraduate students, and teaching of tutorials, Department of Human Metabolism and Clinical Biochemistry, University of Sheffield Medical School, England. Presented papers at the meetings of the Medical Research Society, Heberden Society, Bone and Tooth Society and British Connective Tissue Society. Presented lectures at the Symposium on Immunopathology of Chronic Inflammation; Novel Horizons for Therapy at the XV International Congress of Rheumatology, Paris, June 1981, at the International Symposium on Articular Synovium, Bruges, October 1981, at the Workshop on Immunopharmacology, Hoffman-LaRoche, Nutley, NJ, February, 1982, at the Cologne Atherosclerosis Conference, May, 1982; at the Symposium on Crystal Diseases, Newcastle-upon Tyne, November 1981; and at the Gordon Conferences on Bones and Teeth, July, 1981.

1982-1983 Assisted and collaborated in research programs of arthritis and orthopaedic fellows and foreign visitors in the Arthritis Research Laboratory. Participated and reported in Journal Club sessions. Presented seminars to the Arthritis Research, Orthopedic Research and Developmental Biology Departments at the Massachusetts General Hospital, the Orthopedic Research Department at Tufts University Medical School.

1984-1985 Presented papers at the Annual Meetings of the American Rheumatism Association in Minneapolis, June, 1984 and in Anaheim, CA, June, 1985, the American Society for Bone and Mineral Research, Washington, D.C., June 1985, the Midwest Connective Tissue Society, Chicago, IL, October, 1985, Presented lectures at the Division of Cell and Developmental Biology at Harvard Medical School, Nov. 1985.

1986 Presented papers at the Symposium on Proteases: Their Involvement in Osteoarthritis, Val David, Quebec, Canada, August, 1986; the Orthopedic Research Department at Children's Hospital, October 1986.

1987 Presented lectures at the MGH research Symposium XI, Jan. 1987; the Dept. of Immuno-pharmacology, Hoffman-LaRoche, Inc., October, 1987.

1988 Presented a lecture at the Symposium Roussel UCLAF "Promising Therapeutic Applications of Interleukin-1 and its Antagonists", Paris, France, January, 1988; Rheumatology Grand Rounds, Brigham and Women's Hospital, October, 1988.

1989 Presented lecture for the course on Oral Biology of Connective and Mineralized Tissues, Harvard School of Dental Medicine, April, 1989.

1990 Presented lecture at the conference on Advances in Mineral Metabolism, Snowmass, CO, April 1990. Presented seminars at the Dept. of Anatomy and Cellular Biology, Tufts University School of Medicine, and Depts of Biochemistry and Orthopedic Research, University of Washington, Seattle, April 1990. Presented lecture at the Cartilage Study Group and paper at the American College of Rheumatology, Seattle, October, 1990.

1991 Presented lectures at Merck, West Point, PA, and Genentech, South San Francisco, CA, March, 1991, and at a symposium on "Selective Inhibition of Prostaglandins and Antirheumatic Therapy" sponsored by the Mexican Society of Rheumatology and Wyeth, Mexico City, April 27; discussant at Scientific Workshop on The Biology and Pathology of Acquired Connective Tissue Diseases, National Institute of Arthritis and Musculoskeletal and Skin Diseases, October 28-29; presented work-in progress seminar, Center for the Study of Inflammatory Bowel Disease, MGH, Dec., 1991.

1992 Presented lectures at the 1992 Winter Rheumatology Symposium and the 7th Annual meeting of Advances in Mineral Metabolism; seminars at the University of Miami Medical School, Endocrinology Division and at MIT, Division of Health Sciences Technology; oral presentations at the American Society for Bone and Mineral Research and American College of Rheumatology Annual Meetings.

1993 Presented paper at the Orthopaedic Research Society Annual Meeting; papers at plenary session and concurrent session at American College of Rheumatology. Presented seminars at the Division of Rheumatology,

Thomas Jefferson University Medical College, Philadelphia, and at Pfizer Research. Presented lecture at IBC Conference on "Transcriptional Regulation: Novel Drug Screening & Therapeutics Development"

1994 Presented seminars at Rheumatogy Rounds, Tufts University School of Medicine; at the Oral Biology Seminar Series, the University of Texas Dental School, Health Science Center at San Antonio, Arthritis Grand Rounds, MGH; IBC Symposium on Osteoarthritis, Washington, D.C; Merck Research, Rahway, NJ. Presented papers at the Flims (Switzerland) Panel on Clinical Development of Disease-Controlling Antirheumatic Therapies: Concepts and Strategies, sponsored by Hoffmann-LaRoche; the Misoprostol Research Symposium sponsored by SEARLE; the American College of Rheumatology; the Osteoarthritis Research Society.

1995 Presented seminars at Biochemistry Lecture Series, Boston University; at the Dept. of Orthopedic Surgery, Mayo Clinic, Rochester, MN; at SmithKline Beecham, King of Prussia, PA; presented talks at the Collagen Gordon Conference, American College of Rheumatology.

1996 Presented seminars at Arthritis Grand Rounds, MGH; at St. Francis Hospital & Medical Center (UConn); at the Dept. of Orthopaedic Surgery, Washington Univ., St. Louis; at Ciba-Geigy Corp., Summit, NJ; at Vertex Pharmaceuticals, Inc., Cambridge, MA; at Creative Biomolecules, Hopkinton, MA; at the Nagasaki University School of Medicine, Japan. Presented talk at Orthopaedic Research Society. Presented invited lectures at the 3rd International Congress on Research and Therapeutics in Osteoarthritis, Cannes, France; at the American Society of Rheumatology (Chair of Basic Science Research Symposium: Molecular Mechanisms in the Pathogenesis of Osteoarthritis).

1997 Presented invited lectures at the 3rd International Congress of the Osteoarthritis Research Society, Singapore; the Gordon Research Conference on Collagen; the 9th Conference & Workshop, Texas Mineralized Tissues Society, Corpus Christi, TX.

1998 Presented invited lectures at the Second Workshop on COX-2, Maui, Hawaii; the OARS Workshop on NO & COX in Osteoarthritis, Florence, Italy; IBCUK Conference on Chronic Inflammation, London. Presented seminars at Monsanto Company, St. Louis, MO; Presented short talk at the 2nd Symposium, International Cartilage Repair Society, Boston, MA.

1999 Invited lecture at 4th World Congress on Inflammation, Paris, France (June)

2000 Presented seminar at Arthritis Grand Rounds, UMass Medical School, Worcester, MA. (To be completed)

2001 To be completed

2002 To be completed